

PATENT COOPERATION TREATY

Records 25/11/04
LD on Comp 25/11/04
In Diary 2

From the INTERNATIONAL SEARCHING AUTHORITY

PCT

To:

BOULT WADE TENNANT
Attn. Baldock, Sharon Claire
Verulam Gardens
70 Gray's Inn Road
London WC1X 8BT
UNITED KINGDOM

RECEIVED

25 NOV 2004

BOULT WADE TENNANT

NOTIFICATION OF TRANSMITTAL OF
THE INTERNATIONAL SEARCH REPORT AND
THE WRITTEN OPINION OF THE INTERNATIONAL
SEARCHING AUTHORITY, OR THE DECLARATION

(PCT Rule 44.1)

Applicant's or agent's file reference P72176W000	Date of mailing (day/month/year) 25/11/2004
International application No. PCT/GB2004/004150	FOR FURTHER ACTION See paragraphs 1 and 4 below
Applicant SOLEXA LIMITED	International filing date (day/month/year) 27/09/2004

- 1 ☒ The applicant is hereby notified that the international search report and the written opinion of the International Searching Authority have been established and are transmitted herewith.

Filing of amendments and statement under Article 19:

The applicant is entitled, if he so wishes, to amend the claims of the International Application (see Rule 46):

When? The time limit for filing such amendments is normally 2 months from the date of transmittal of the International Search Report; however, for more details, see the notes on the accompanying sheet.

Where? Directly to the International Bureau of WIPO, 34 chemin des Colombettes
1211 Geneva 20, Switzerland, Facsimile No.: (41-22) 740.14.35

For more detailed instructions, see the notes on the accompanying sheet.

- 2 ☐ The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect and the written opinion of the International Searching Authority are transmitted herewith.

- 3 ☐ **With regard to the protest** against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

- ☐ the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.
☐ no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4 Reminders


Shortly after the expiration of **18 months** from the priority date, the international application will be published by the international Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90bis.1 and 90bis.3, respectively, before the completion of the technical preparations for international publication.

The applicant may submit comments on an informal basis on the written opinion of the International Searching Authority to the International Bureau. The International Bureau will send a copy of such comments to all designated Offices unless an international preliminary examination report has been or is to be established. These comments would also be made available to the public but not before the expiration of 30 months from the priority date.

Within **19 months** from the priority date, but only in respect of some designated Offices, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until **30 months** from the priority date (in some Offices even later); otherwise, the applicant must, **within 20 months** from the priority date, perform the prescribed acts for entry into the national phase before those designated Offices.

In respect of other designated Offices, the time limit of **30 months** (or later) will apply even if no demand is filed within 19 months.

See the Annex to Form PCT/IB/301 and, for details about the applicable time limits, Office by Office, see the *PCT Applicant's Guide*, Volume II, National Chapters and the WIPO Internet site.

Name and mailing address of the International Searching Authority  European Patent Office, P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Authorized officer Angela Lopez Navarro
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NOTES TO FORM PCT/ISA/220

These Notes are intended to give the basic instructions concerning the filing of amendments under article 19. The Notes are based on the requirements of the Patent Cooperation Treaty, the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the PCT Applicant's Guide, a publication of WIPO.

In these Notes, "Article", "Rule", and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions respectively.

INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international publication. Furthermore, it should be emphasized that provisional protection is available in some States only.

What parts of the international application may be amended?

Under Article 19, only the claims may be amended.

During the international phase, the claims may also be amended (or further amended) under Article 34 before the International Preliminary Examining Authority. The description and drawings may only be amended under Article 34 before the International Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

When?

Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

Where not to file the amendments?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been/is filed, see below.

How?

Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Administrative Instructions, Section 205(b)).

The amendments must be made in the language in which the international application is to be published.

What documents must/may accompany the amendments?

Letter (Section 205(b)):

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

The letter must be in English or French, at the choice of the applicant. However, if the language of the international application is English, the letter must be in English; if the language of the international application is French, the letter must be in French.

NOTES TO FORM PCT/ISA/220 (continued)

The letter must indicate the differences between the claims as filed and the claims as amended. It must, in particular, indicate, in connection with each claim appearing in the international application (it being understood that identical indications concerning several claims may be grouped), whether

- (i) the claim is unchanged;
- (ii) the claim is cancelled;
- (iii) the claim is new;
- (iv) the claim replaces one or more claims as filed;
- (v) the claim is the result of the division of a claim as filed.

The following examples illustrate the manner in which amendments must be explained in the accompanying letter:

1. [Where originally there were 48 claims and after amendment of some claims there are 51]:
"Claims 1 to 29, 31, 32, 34, 35, 37 to 48 replaced by amended claims bearing the same numbers; claims 30, 33 and 36 unchanged; new claims 49 to 51 added."
2. [Where originally there were 15 claims and after amendment of all claims there are 11]:
"Claims 1 to 15 replaced by amended claims 1 to 11."
3. [Where originally there were 14 claims and the amendments consist in cancelling some claims and in adding new claims]:
"Claims 1 to 6 and 14 unchanged; claims 7 to 13 cancelled; new claims 15, 16 and 17 added." or
"Claims 7 to 13 cancelled; new claims 15, 16 and 17 added; all other claims unchanged."
4. [Where various kinds of amendments are made]:
"Claims 1-10 unchanged; claims 11 to 13, 18 and 19 cancelled; claims 14, 15 and 16 replaced by amended claim 14; claim 17 subdivided into amended claims 15, 16 and 17; new claims 20 and 21 added."

"Statement under article 19(1)" (Rule 46.4)

The amendments may be accompanied by a statement explaining the amendments and indicating any impact that such amendments might have on the description and the drawings (which cannot be amended under Article 19(1)).

The statement will be published with the international application and the amended claims.

It must be in the language in which the international application is to be published.

It must be brief, not exceeding 500 words if in English or if translated into English.

It should not be confused with and does not replace the letter indicating the differences between the claims as filed and as amended. It must be filed on a separate sheet and must be identified as such by a heading, preferably by using the words "Statement under Article 19(1)."

It may not contain any disparaging comments on the international search report or the relevance of citations contained in that report. Reference to citations, relevant to a given claim, contained in the international search report may be made only in connection with an amendment of that claim.

Consequence if a demand for international preliminary examination has already been filed

If, at the time of filing any amendments under Article 19, a demand for international preliminary examination has already been submitted, the applicant must preferably, at the same time of filing the amendments with the International Bureau, also file a copy of such amendments with the International Preliminary Examining Authority (see Rule 62.2(a), first sentence).

Consequence with regard to translation of the international application for entry into the national phase

The applicant's attention is drawn to the fact that, where upon entry into the national phase, a translation of the claims as amended under Article 19 may have to be furnished to the designated/elected Offices, instead of, or in addition to, the translation of the claims as filed.

For further details on the requirements of each designated/elected Office, see Volume II of the PCT Applicant's Guide.

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference P72176W000	FOR FURTHER ACTION <small>see Form PCT/ISA/220 as well as, where applicable, item 5 below.</small>	
International application No. PCT/GB2004/004150	International filing date (day/month/year) 27/09/2004	(Earliest) Priority Date (day/month/year) 25/09/2003
Applicant SOLEXA LIMITED		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 7 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ The international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. ☐ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2. ☒ **Certain claims were found unsearchable** (See Box II).

3. ☐ **Unity of invention is lacking** (see Box III).

4. With regard to the title,

☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:

5. With regard to the abstract,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. With regards to the drawings,

- a. the figure of the **drawings** to be published with the abstract is Figure No. _____

☐ as suggested by the applicant.

☐ as selected by this Authority, because the applicant failed to suggest a figure.

☐ as selected by this Authority, because this figure better characterizes the invention.

- b. ☒ none of the figures is to be published with the abstract.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/GB2004/004150

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07C63/307 C07D207/46 C07D209/48 C07D211/94 C07C57/34
C07C57/72 G01N33/543

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 G01N C07C C07D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic database consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, BEILSTEIN Data, WPI Data, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

with indication, where appropriate, of the relevant passages

Relevant to claim No.

X DATABASE CA 'Online!
CHEMICAL ABSTRACTS SERVICE, COLUMBUS,
OHIO, US;
accession no. 135:344649
D.K. ET AL: "Synthesis and
binding properties of cyclodextrin
trimers" TETRAHEDRON LETTERS,
vol. 42, no. 36, 2001, pages 6255-6258,

38

X DATABASE CA 'Online!
CHEMICAL ABSTRACTS SERVICE, COLUMBUS,
OHIO, US;
XP002270049
Database accession no. 130:259811
abstract
-/--

38

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

Z document member of the same patent family

Date of the actual completion of the international search

18 November 2004

Date of mailing of the international search report

25/11/2004

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Österle, C

INTERNATIONAL SEARCH REPORT

 International Application No
 PCT/GB2004/004150

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	& PODLAHA, J. ET AL: "Crystal structure of 1,2,3,4,5,6-hexakis(2'-carboxyethyl)benzene dihydrate, C ₂₄ H ₃₀ O ₁₂ ·2H ₂ O" ZEITSCHRIFT FÜR KRISTALLOGRAPHIE-NEW CRYSTAL STRUCTURES, vol. 214, no. 2, 1999, pages 183-184, ----- DATABASE CA 'Online! CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; XP002270050 Database accession no. 127:333050 abstract & SPINO, C. ET AL: "Lanthanide catalysts for the hetero Diels-Alder reaction: effect of ligand structure and acidity" CANADIAN JOURNAL OF CHEMISTRY, vol. 75, no. 8, 1997, pages 1047-1054, -----	38
X	DATABASE CA 'Online! CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; XP002270051 Database accession no. 98:197855 abstract & COLLMAN, JAMES P. ET AL: J.AM.CHEM.SOC., vol. 105, no. 10, 1983, pages 3038-3052, -----	38
X	DATABASE CA 'Online! CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; XP002270052 Database accession no. 96:104214 abstract & KANISHI, M. ET AL: "Synthesis of macrocyclic 'n.n.n!(1,3,5)cyclophane polylactones" BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN, vol. 54, no. 12, 1981, pages 3828-3831, -----	38
X	COLLMAN, J.P. ET AL: "Synthesis and characterization of the "pocket" porphyrins" J.AM.CHEM.SOC., vol. 105, no. 10, 1983, pages 3038-3052, XP002270041 *scheme I* ----- -/--	38

INTERNATIONAL SEARCH REPORT

 International Application No
 PCT/GB2004/004150

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	SIGMAN, M.S. ET AL: "Cobalt-catalyzed cyclotrimerization of alkynes in aqueous solution" J.AM.CHE.SOC., vol. 120, no. 20, 1998, pages 5130-5131, XP002270042 *p. 5131, compounds 18a and 18b*	38, 39
X	DATABASE CROSSFIRE BEILSTEIN 'Online! Beilstein Institut zur Förderung der chemischen Wissenschaften, Frankfurt am Main, DE; XP002270053 Database accession no. 4435562 (BRN) abstract & HOFFMANN, H.M.R. ET AL: SYNTHESIS, vol. 3, 1982, pages 237-239,	38, 39
X	DATABASE CROSSFIRE BEILSTEIN 'Online! Beilstein Institut zur Förderung der chemischen Wissenschaften, Frankfurt am Main, DE; XP002270054 Database accession no. 3361499 (BRN) abstract & HOPFF ET AL: HELV.CHIM.ACTA, vol. 40, 1957, pages 274-280,	38, 39
X	COLQUHOUN, H.M. ET AL: "One-step synthesis of very large cage-type molecules from aromatic sub-units" CHEM.COMMUN., 2001, pages 2574-2575, XP002270043 *compounds 2 and 6*	38
X	NEWMAN, M.S. ET AL: "The synthesis of 1,3,5-Benzenetriacetic acid by a triple-Willgerodt reaction" J.AM.CHEM.SOC., vol. 76, 1954, pages 6196-6197, XP002270044 *the whole document*	38, 39
X	WENKERT, E. ET AL: "Derivatives of Hemimellitic Acid. A synthesis of Erythrocentaurin" J.AM.CHEM.SOC., vol. 29, 1964, pages 2534-2542, XP002270045 *compound 1a, 4a, 4c, 7k*	38, 39

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB2004/004150

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	"Aldrich-Handbuch Feinchemikalien" 1999, ALDRICH, XP002270047 *catalog numbers: B420-1, B458-9, 48,274-9, B460-0, T6,802-0,14,753-2* page 179 - page 180	38
X	HANESSIAN, S. ET AL: "Design and synthesis of a cephalosporin-carboplatinum prodrug activatable by a beta-lactamase" CAN.J.CHEM., vol. 71, 1993, pages 896-906, XP0009025793 *compounds 3-7, p. 897*	38, 39
A	EP 0 280 840 A (PALL CORP) 7 September 1988 (1988-09-07) page 6, line 35 - page 7, line 20- claims	12-24
A	PIRRUNG M C ET AL: "A General Method for the Spatially Defined Immobilization of Biomolecules on Glass Surfaces Using Caged Biotin" BIOCONJUGATE CHEMISTRY, AMERICAN CHEMICAL SOCIETY, WASHINGTON, US, vol. 7, no. 3, May 1996 (1996-05), pages 317-321, XP002095758 ISSN: 1043-1802 cited in the application *the whole document*	1-37
A	ADESSI C ET AL: "Solid phase DNA amplification: characterization of primer attachment and amplification mechanisms" NUCLEIC ACIDS RESEARCH, OXFORD UNIVERSITY PRESS, SURREY, GB, vol. 28, no. 20, 15 October 2000 (2000-10-15), page e87, XP002169484 ISSN: 0305-1048 cited in the application *the whole document*	1-37
A	PIRRUNG M C: "HOW TO MAKE A DNA CHIP" ANGEWANDTE CHEMIE. INTERNATIONAL EDITION, VERLAG CHEMIE. WEINHEIM, DE, vol. 41, no. 8, 2002, pages 1277-1289, XP001111695 ISSN: 0570-0833 cited in the application page 1278; table 1	1-37
A	US 4 140 662 A (RECKEL RUDOLPH P ET AL) 20 February 1979 (1979-02-20) cited in the application *the whole document*	1-37

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/GB2004/004150

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 6 319 674 B1 (DELLINGER DOUGLAS J ET AL) 20 November 2001 (2001-11-20) *the whole document* -----	1-37

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/GB2004/004150

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
EP 0280840	A	07-09-1988	US 4693985 A	15-09-1987
			EP 0280840 A1	07-09-1988
			CA 1249781 A1	07-02-1989
			DE 3573886 D1	30-11-1989
			DE 3585542 D1	09-04-1992
			EP 0173500 A1	05-03-1986
			GB 2163434 A ,B	26-02-1986
			GB 2199327 A ,B	06-07-1988
			JP 1963000 C	25-08-1995
			JP 6089169 B	09-11-1994
			JP 61124868 A	12-06-1986
US 4140662	A	20-02-1979	AR 217685 A1	15-04-1980
			AT 361636 B	25-03-1981
			AT 213578 A	15-08-1980
			AU 3431278 A	27-09-1979
			BE 865195 A1	22-09-1978
			BR 7801779 A	19-12-1978
			CA 1089764 A1	18-11-1980
			DE 2812845 A1	28-09-1978
			DK 128078 A	26-09-1978
			ES 467190 A1	01-08-1979
			FR 2384789 A1	20-10-1978
			GB 1600434 A	14-10-1981
			IT 1111074 B	13-01-1986
			JP 53118517 A	17-10-1978
			NL 7803209 A	27-09-1978
			NO 781039 A	26-09-1978
			NZ 186763 A	26-08-1980
			SE 7803241 A	26-09-1978
			ZA 7801719 A	28-11-1979
US 6319674	B1	20-11-2001	NONE	

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

PCT

see form PCT/ISA/220

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/GB2004/004150

International filing date (day/month/year)
27.09.2004

Priority date (day/month/year)
25.09.2003

International Patent Classification (IPC) or both national classification and IPC
C07C63/307, C07D207/46, C07D209/48, C07D211/94, C07C57/34, C07C57/72, G01N33/543

Applicant
SOLEXA LIMITED

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1b(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:



European Patent Office
D-80298 Munich
Tel. +49 89 2399 - 0 Tx: 523656 epmu d
Fax: +49 89 2399 - 4465

Authorized Officer

Österle, C

Telephone No. +49 89 2399-8120



40/573377

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/GB2004/004150

IAP20 Rec'd PCT/PTO 27 MAR 2006

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
 - ☐ This opinion has been established on the basis of a translation from the original language into the following language, which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material
 - ☐ Sequence listing
 - ☐ Table related to the sequence listing
 - b. format of material
 - ☐ In machine readable form
 - ☐ In human readable form
 - c. time of filing (if applicable)
 - ☐ Contained in the international application as filed.
 - ☐ Filed together with the international application in computer readable form.
 - ☐ Furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/GB2004/004150

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application,
- ☒ claims Nos. 1-11,13-16,20-39 all in part

because:

- ☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):
- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- ☒ no international search report has been established for the whole application or for said claims Nos. 1-11,13-16,20-39 all in part
- ☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:
 - the written form ☐ has not been furnished
 - ☐ does not comply with the standard
 - the computer readable form ☐ has not been furnished
 - ☐ does not comply with the standard
- ☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.
- ☐ See separate sheet for further details



**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/GB2004/004150

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	1-37
	No: Claims	38,39
Inventive step (IS)	Yes: Claims	17-19
	No: Claims	1-16,20-39
Industrial applicability (IA)	Yes: Claims	1-39
	No: Claims	

2. Citations and explanations

see separate sheet

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING
AUTHORITY (SEPARATE SHEET)**

40/573377

International application No.

PCT/GB2004/004150

1AP20 Rec'd PCT/PTO 27 MAR 2006

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The subject-matter of claims 1-16 and 20-39 has only been subject to an international search as the compounds these claims relate to are compounds for which the at least three of R1 to R6 are R1, R3 and R5. Claims or parts of claims for which an international search report has not been established are not subject of international preliminary examination. The opinion below therefore only relates to parts of the claims which have been searched.

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

- D1: DATABASE CA [Online] CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; Database accession no. 135:344649 XP002270048 & LEUNG, D.K. ET AL: 'Synthesis and binding properties of cyclodextrin trimers' TETRAHEDRON LETTERS, vol. 42, no. 36, 2001, pages 6255-6258,
- D2: DATABASE CA [Online] CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; Database accession no. 130:259811 XP002270049 & PODLAHA, J. ET AL: 'Crystal structure of 1,2,3,4,5,6-hexakis(2'-carboxyethyl)benzene dihydrate, C₂₄H₃₀O₁₂.2H₂O' ZEITSCHRIFT FÜR KRISTALLOGRAPHIE-NEW CRYSTAL STRUCTURES, vol. 214, no. 2, 1999, pages 183-184,
- D3: DATABASE CA [Online] CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; Database accession no. 127:333050 XP002270050 & SPINO, C. ET AL: 'Lanthanide catalysts for the hetero Diels-Alder reaction: effect of ligand structure and acidity' CANADIAN JOURNAL OF CHEMISTRY, vol. 75, no. 8, 1997, pages 1047-1054,
- D4: DATABASE CA [Online] CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; Database accession no. 98:197855 XP002270051 & COLLMAN, JAMES P. ET AL: J.AM.CHEM.SOC., vol. 105, no. 10, 1983, pages 3038-3052,
- D5: DATABASE CA [Online] CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; Database accession no. 96:104214 XP002270052 & KANISHI, M. ET AL:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING
AUTHORITY (SEPARATE SHEET)**

International application No.

PCT/GB2004/004150

- 'Synthesis of macrocyclic [n.n.n](1,3,5)cyclophane polylactones' BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN, vol. 54, no. 12, 1981, pages 3828-3831,
- D6: COLLMAN, J.P. ET AL: 'Synthesis and characterization of the 'pocket' porphyrins' J.AM.CHEM.SOC., vol. 105, no. 10, 1983, pages 3038-3052, XP002270041
- D7: SIGMAN, M.S. ET AL: 'Cobalt-catalyzed cyclotrimerization of alkynes in aqueous solution' J.AM.CHE.SOC., vol. 120, no. 20, 1998, pages 5130-5131, XP002270042
- D8: DATABASE CROSSFIRE BEILSTEIN [Online] Beilstein Institut zur Förderung der chemischen Wissenschaften, Frankfurt am Main, DE; Database accession no. 4435562 (BRN) XP002270053 & HOFFMANN, H.M.R. ET AL: SYNTHESIS, vol. 3, 1982, pages 237-239,
- D9: DATABASE CROSSFIRE BEILSTEIN [Online] Beilstein Institut zur Förderung der chemischen Wissenschaften, Frankfurt am Main, DE; Database accession no. 3361499 (BRN) XP002270054 & HOPFF ET AL: HELV.CHIM.ACTA, vol. 40, 1957, pages 274-280,
- D10: COLQUHOUN, H.M. ET AL: 'One-step synthesis of very large cage-type molecules from aromatic sub-units' CHEM.COMMUN., 2001, pages 2574-2575, XP002270043
- D11: NEWMAN, M.S. ET AL: 'The synthesis of 1,3,5-Benzenetriacetic acid by a triple-Willgerodt reaction' J.AM.CHEM.SOC., vol. 76, 1954, pages 6196-6197, XP002270044
- D12: WENKERT, E. ET AL: 'Derivatives of Hemimellitic Acid. A synthesis of Erythrocentaurin' J.AM.CHEM.SOC., vol. 29, 1964, pages 2534-2542, XP002270045
- D13: 'Aldrich-Handbuch Feinchemikalien' 1999 , ALDRICH XP002270047
- D14: HANESSIAN, S. ET AL: 'Design and synthesis of a cephalosporin-carboplatinum prodrug activatable by a beta-lactamase' CAN.J.CHEM., vol. 71, 1993, pages 896-906, XP002270046
- D15: US-B-6 319 6741 (DELLINGER DOUGLAS J ET AL) 20 November 2001 (2001-11-20)

1. Article 6 PCT:

- 1.1 Claim 39 does not disclose the technical features necessary to carry out the invention and therefore lacks clarity.

2. Novelty (Article 33(2) PCT):

- 2.1 The subject-matter of claims 38 and 39 is anticipated by D1-D14 (see passages cited in the search report).
- 2.2 The documents cited in the search report do not disclose the method of claims 1-31 and claims 34-37 or the solid surface of claims 32 and 33.

The subject-matter of claims 1-37 therefore can be considered novel.

3. Inventive Step (Article 33(3) PCT):

- 3.1 The technical problem to be solved by the present application is to provide compounds with which a solid support comprising amine groups can be derivatized such that biomolecules comprising amine groups can be linked to said support.

The solution suggested by the applicant are the compounds of present claim 38.

In the description on p. 4-6 the advantages of the present invention as compared to the prior art are disclosed.

The advantages, among others, are the increased amount of carboxyl groups available for covalent attachment of biomolecules and the decreased flexibility of the molecules, leading to less secondary reactions of the linker with the solid surface.

Not all compounds of present claim 38 seem to have this technical effect:

In order to be suitable as linkers, the at least three of R1 to R6 being other than H have to be R1, R3 and R5. If the three substituents would be R1, R2 and R3, all carboxyl groups would be close to the solid support, unavailable for covalent attachment of biomolecules.

Not all compounds of present claim 38 therefore are considered to have the desired technical effect.

Present claim 38 then does not fulfil the requirements of Article 33(3) PCT.

- 3.2 The same argumentation as under 3.1 also applies to claims 2-16, 20-37 and 39 mutatis mutandis.
- 3.3 In claims 17-19 the compounds used in the method are compounds for which the at least three R1-R6 are R1, R3 and R6. The methods of claims 17-19 therefore are considered to solve the technical problem.

D15 also discloses a method for modifying a solid support such that substances can be immobilized on this surface. In D15, a silicon surface is derivatized with an alkyl bromide which then, in a further step is derivatized with an ethylene glycol linker. The derivatized surface then can react with for example an oligonucleotide. D15 does not disclose the derivatization of a surface such that more than one further molecule can be attached to the linker group.

The subject-matter of claims 17-19 then can also be considered inventive in view of the closest prior art.

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